Microbiome Changes a Markers of Exposure and Stress in Firefighters

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Inherent risks in Firefighting Profession

- Several diseases such as respiratory, cardiovascular, hypertension have been linked to occupational exposures

- Firefighters are regularly subjected to heat exposures and stress which involve inhalation of carcinogenic and pro-inflammatory chemicals such as PAHs and particulates

- These exposures have been linked to Respiratory and systemic pathologies

- Some of the respiratory conditions are common to those seen in Smokers and people with dental diseases such as periodontitis etc.

A firefighter in action
(Source: mentalfloss.com)

NORA RELEVANCE

- In NORA research agenda, there is <u>continuing interest to identify specific etiological agents/factors</u> for occupational diseases in high risk professions including firefighters.

- Occupational diseases in firefighters such as pulmonary and cardiovascular diseases, diabetes, and cancer are in <u>the top priority areas of research for NIOSH</u>.
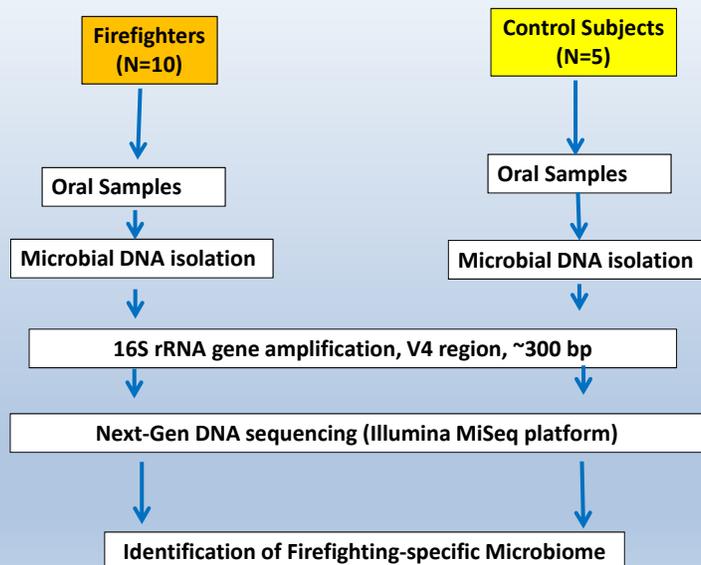
Microbiome hypothesis

Firefighters frequently inhale smoke constituents (Particulates and toxicants such as PAHs and other carcinogenic chemicals) and get exposed to heat stress while fighting fires. This may alter their microbiome and result in health effects.

We therefore <u>hypothesized</u> that occupational exposure during firefighting events can alter the physiological homeostasis in firefighters in terms of altered mucosal microbiome (e.g. oral or gut microbiota)

Specific Aims

- <u>Characterize microbiome</u> in firefighters versus Normal control individuals using Nextgen DNA sequencing

- Identify <u>microbiome x metadata interactions</u> in firefighters using bioinformatic and statistical analyses

Experimental Flowsheet

Firefighters (N=10)		Control Subjects (N=5)
↓		↓
Oral Samples		Oral Samples
↓		↓
Microbial DNA isolation		Microbial DNA isolation

16S rRNA gene amplification, V4 region, ~300 bp

Next-Gen DNA sequencing (Illumina MiSeq platform)

Identification of Firefighting-specific Microbiome

INTEGRATED ANALYSIS

MICROBIOME
- Recovery of microorganisms from oral samples

- DNA Extraction

- Nextgen sequencing (NGS)

  – 16S-rDNA V4 region targeted (300 bp)

  – Barcode based amplification

  – Next-gen sequencing using Illumina Miseq platform
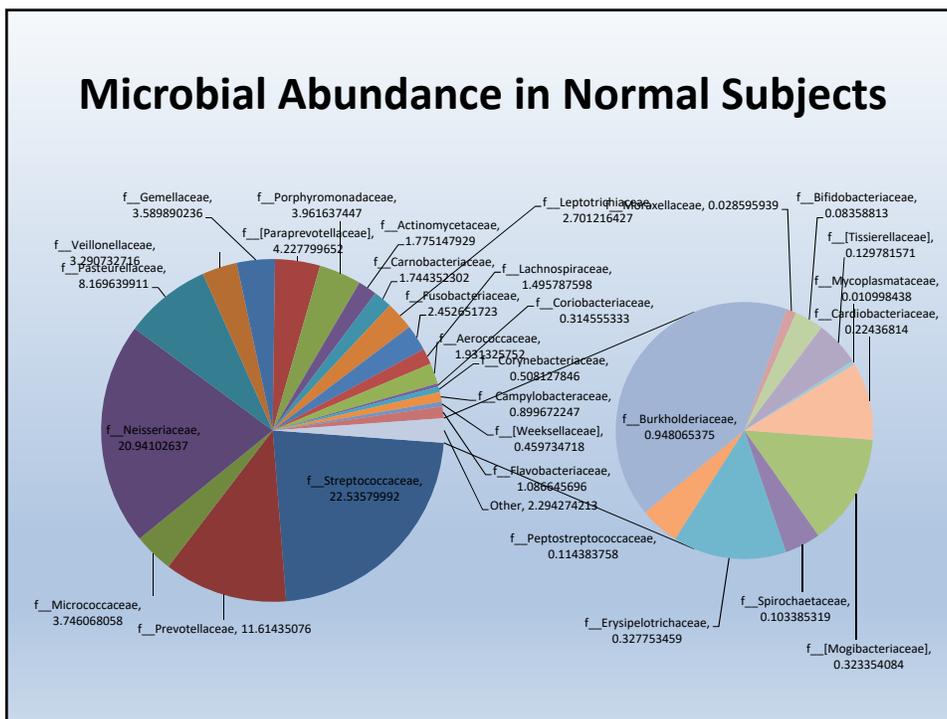
  – Bioinformatic analysis using Mothur (version 1.36.1)

METADATA
- Collection of metadata using study questionnaire.
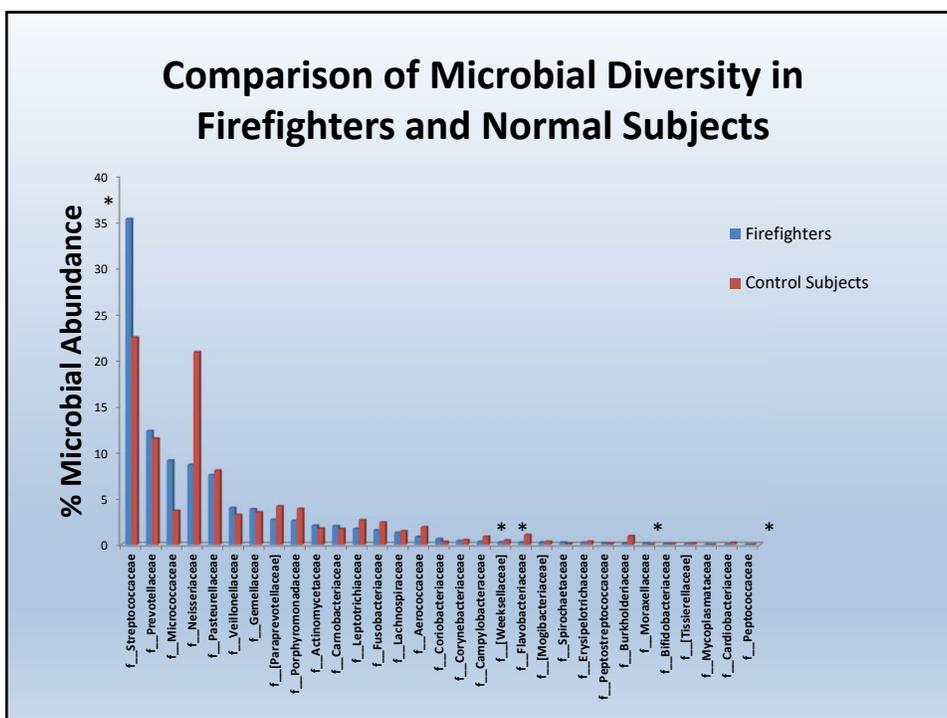- Statistical analysis for integration with microbiome data
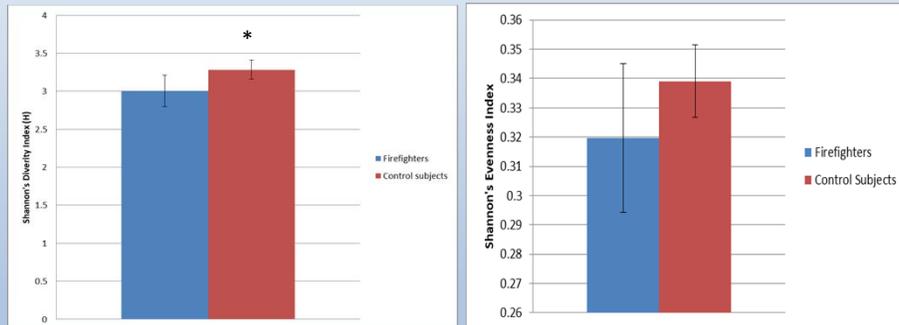

Microbial Abundance in Firefighters
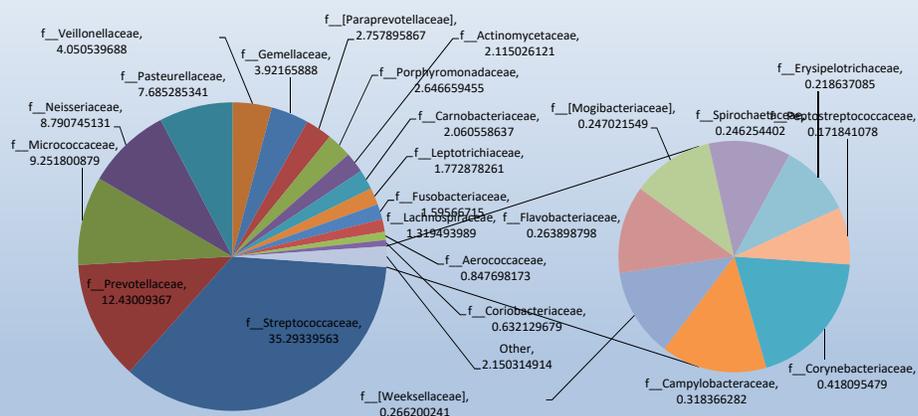
Microbial Abundance in Normal Subjects

Comparison of Microbial Diversity in Firefighters and Normal Subjects

Shannon's Diversity and Evenness Indices for Firefighters and Control Subjects

Metadata x Microbiome Interactions in Firefighters

Metadata	Microbiome Change	P-Value
Firefighting experience (> 5 yrs)	↑PeptoStreptococcaceae	0.035*
Fire events (>20)	↑PeptoStreptococcaceae	0.035*
Food PAH intake (past 8 hrs)	↑Veillonellaceae ↑Actinomycetaceae ↑Peptostreptococcaceae	0.095
Tobacco usage within past 8 hrs	↑Streptococcaceae ↑Veillonellaceae ↑Gemellaceae ↑Actinomycetaceae ↑Peptostreptococcaceae ↑Peptococcaceae	0.095 0.078

SUMMARY

- Firefighters group showed considerably <u>increased proportion of</u> bacterial families particularly *Streptococaceae (p ≤ 0.05), Prevotellaceae,* and *Micrococcaceae*

- Firefighters group showed a significantly <u>decreased proportion of</u> families particularly *Neisseriaceae, Campylobacteriaceae (p ≤ 0.05), Weeksellaceae (p ≤ 0.05), Burkholderiaceae (p ≤ 0.05), Cardiobacteriaceae (p ≤ 0.05).*

- Overall, firefighters showed an <u>altered oral microbiome both in terms of proportion and count</u> of multiple individual components.

- Integrated analyses with questionnaire based metadata implied that some of the <u>compounding factors related to exposure and lifestyle</u> may have significant (P> 0.05) or close to significant impact on the microbiome perturbations in firefighters.

Work in Progress …

- Further sampling of firefighters for systemic mucosal microbiome.

- Larger sampling efforts for gaining further insights and power into microbiome x metadata interactions

- Setting up Mouse Exposure models to understand the crosstalk between toxicants (e.g. PAHs) and microbiome components

Impact Statement

This study on Microbiome changes in firefighters will help understand the following in long term….

- <u>Microbiome biomarkers</u> for firefighting-related exposure assessment and health effects (**r2P potential**)

- Role of microbiome <u>dysbiosis in predisposing</u> firefighters to occupational health risks

- <u>Etiological factors</u> for firefighting-related diseases

- Possible <u>intervention strategies</u> (dietary, PPE, etc)

The data obtained will support our ongoing efforts for future research funding…

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Questions ?